Original Article

Correlation between Frailty and Cognitive Function in Non-Demented Community Dwelling Older Koreans

Sun Kim, Jun Li Park, Hwan Sik Hwang[1], Yeon Pyo Kim*

Department of Family Medicine, Chonnam National University Hwasun Hospital, Hwasun; [1]Department of Family Medicine, Hanyang University College of Medicine, Seoul, Korea

Background: Frailty and cognitive impairment are considered the most common and yet least understood conditions in older adults. This study was conducted to investigate the correlation between frailty and cognitive function in non-demented older Koreans.

Methods: Korean Mini-Mental Status Examination (K-MMSE) scores and Cardiovascular Health Study Frailty Indices were obtained for 486 older adults aged 65 and over who registered at six senior welfare centers in Seoul and Gyeonggi province. Multiple linear regression was performed to identify the association between frailty and K-MMSE scores.

Results: Of the 486 older adults, 206 (42.4%) were robust, 244 (50.2%) were prefrail, and 36 (7.4%) were frail. Prevalence of cognitive impairment (K-MMSE ≤ 23) was 6.3% in the robust group, 16.8% in the prefrail group, and 30.6% in the frail group ($P < 0.001$), and mean K-MMSE score was 27.5 ± 2.2, 26.5 ± 3.1, and 23.7 ± 5.3, respectively ($P < 0.001$). Frailty tended to be associated with lower MMSE scores (B = –1.92, standard error, 0.52; $P < 0.001$).

Conclusion: Frailty was found to be correlated with cognitive impairment in non-demented older Koreans. However, further cohort studies are required to determine the association between frailty and cognitive function.

Keywords: Aging; Frail Elderly; Cognition; Koreans

INTRODUCTION

South Korea faces a challenge posed by a rapidly growing older population (>65 years old), which increased from 7.2% of the total population in 2000 to 11% in 2010. Furthermore, this growth is expected to continue to 14.3% in 2018 and 20.8% in 2026.[1,2] Increases in older populations can cause economic and medical burdens associated with taking care of dependent older adults with physical or mental impairments,[3] and frailty and cognitive impairment are considered as the most common and yet least understood conditions in older adults.[3]

Frailty is an age-related reduction in the ability to respond to stressors and increased vulnerability to weakness, morbidity, disability, and death.[4] No consensus has been reached regarding the definition of frailty but two types of operational definitions have been commonly used.[3] Rockwood et al.[5] proposed the Cumulative Burden Index that frailty that be defined as an accumulation of health conditions and deficits. Cognitive impairment itself can be included as one of possible deficits. Fried et al.[4] proposed the Biological Syndrome Model that be defined as a condition that

Received: August 14, 2013, Accepted: October 14, 2014

*Corresponding Author: Yeon-Pyo Kim
Tel: +82-61-379-7290, Fax: +82-61-379-7291
E-mail: reusable@hanmail.net

Korean Journal of Family Medicine

satisfies at least three of five objective criteria, that is weight loss, exhaustion, reduced physical activity, reduced gait speed, and weakness. Fried et al.[4] did not include cognitive function in its definition because they suggested that physical frailty was one of causes resulting in adverse outcome as cognitive impairment.

Cognitive impairment describes a decline in intellectual functions, such as, thinking, remembering, reasoning and planning,[3] and ranges from mild forms of forgetfulness to severe and debilitating dementia. Mild cognitive impairment is a state of cognitive decline that is not accompanied by any significant functional disability,[6] but shows a high rate of progression to all types of dementia in which severe cognitive impairment is accompanied by increasing physical decline, eventually leading to full physical dependency.[3]

Several studies provided evidence of a relationship between frailty and cognitive impairment. Avila-Funes et al.[7] reported higher rates of cognitive impairment in frail (22%) than in pre-frail (12%) or robust (10%) older people, and many longitudinal studies have suggested that higher levels of frailty predict cognitive decline[8-10] and incident dementia.[11,12] Samper-Ternent et al.[10] reported that subjects in the frail category showed faster and more severe cognitive decline over 10 years than those in the prefrail category. On the other hand, some studies concluded that cognition was not correlated strongly with frailty, while they define frailty as one concept consisting of physical activity, mobility, energy, strength and mood.[13,14]

If frailty is shown to cause cognitive impairment, interventions to reduce frailty may prevent cognitive decline. Although some studies have been conducted on frailty in older Koreans, the relationship between frailty and cognitive function in older Koreans has received little attention. Hence, we aimed to investigate the correlation between frailty and cognitive function in non-demented community dwelling older Koreans by using data collected during two studies the Validity and Reliability of Korean Frailty Index[15] and the Validity and Reliability of the Kaigo-Yobo Checklist in Korean Elderly.[16]

METHODS

1. Participants

Study population was composed of individuals that

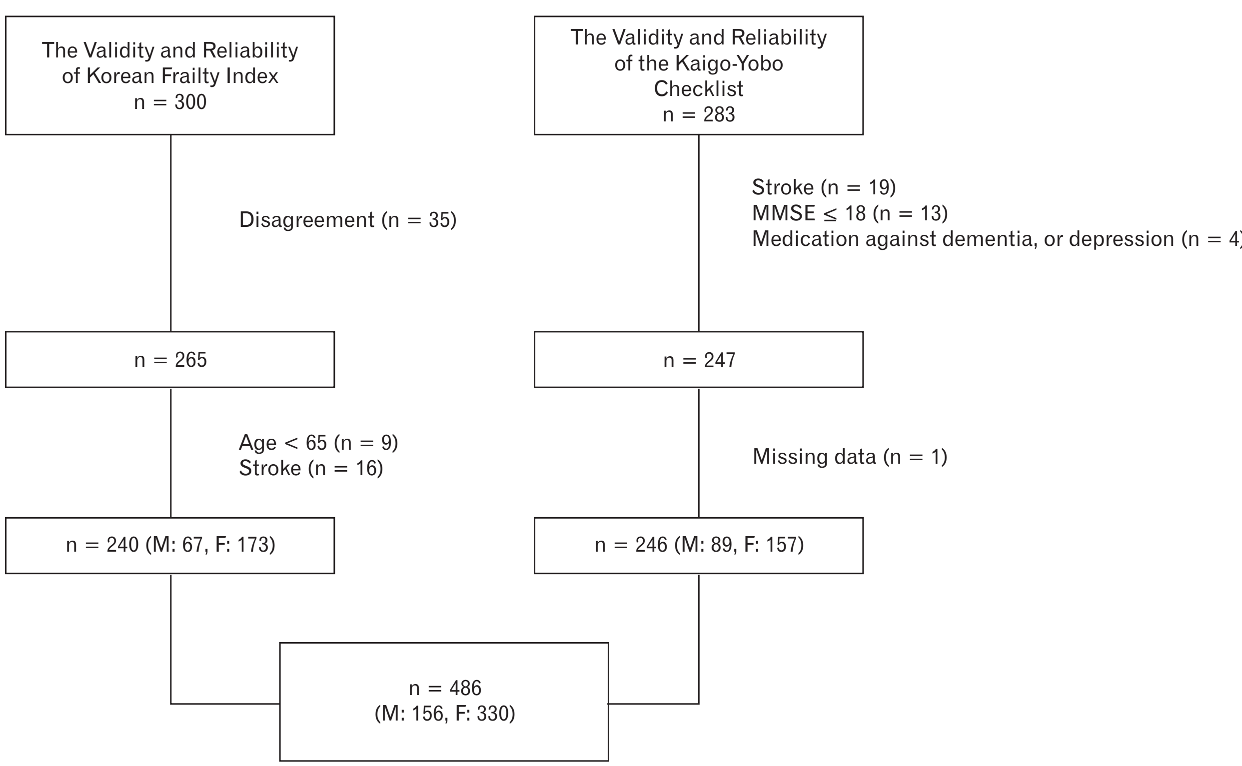

Figure 1. Recruitment of study population.

participated in the Validity and Reliability of Korean Frailty Index[15] and the Validity and Reliability of the Kaigo-Yobo Checklist in Korean Elderly (Figure 1).[16]

In the Validity and Reliability of Korean Frailty Index,[15] initially 300 older adults (≥65 years old), registered at three senior welfare centers located in Seoul were randomly selected. After explaining the purpose of this study, 265 elderly (Sungdong welfare center, n = 53; Sillim welfare center, n = 138; Jung-gu Yoo-Rock welfare center, n = 74), who understood the purposes of the study and provided signed consent, were included. A structured survey and physical examination were performed on these candidate subjects from June 2009 to August 2009. Participants in the survey were limited to those who could understand the survey contents and answer questions adequately. Those unable to stand independently or walk more than 10 meters without assistance due to symptoms that restrict motility, such as, dizziness, a visual disorder, or shortness of breath, were excluded. However, we included individuals who had difficulty reading the questionnaire due to a vision problem or a lack of education by reading the questions to them and filling the questionnaires on their behalf. Patients with Parkinson disease, a previous history of stroke, dementia (a Korean Mini-Mental State Examination [K-MMSE] score of < 18), and patients taking drugs for dementia or depression were excluded. Of the 265 subjects who participated in the original survey, 25 subjects with an age of < 65 (n = 9) or a history of stroke (n = 16) were also excluded. These inclusion and exclusion criteria were adopted from the Cardiovascular Health Study (CHS), as described by Ferrucci et al.[17]

In the validity and reliability of the Kaigo-Yobo checklist in Korean elderly study,[16] 283 older adults (≥65 years old) registered at two senior welfare centers located in Seoul (n = 37 and n = 238) and one senior welfare center in Gyeonggi province (n = 8) were recruited from March, 2011 to May, 2011. According to the exclusion criteria of Ferrucci et al.,[17] 36 subjects were excluded (stroke, n = 19; K- MMSE score < 18, n = 13), and taking drugs for dementia or depression (n = 4). In addition, missing data (n = 1) was also excluded. The study protocols were approved beforehand by the Hanyang University Hospital institutional review board (HYUH IRB No. 2008-R-38 and HYUH IRB No. 2010-R-47).

2. Measures

1) Cognitive function assessment: Korean Mini-Mental State Examination

Cognitive function was assessed using the K-MMSE, the Korean version of Mini-Mental State Examination (MMSE). The MMSE was developed by Folstein in 1975 and has been widely used to measure cognitive function in clinical and research settings.[18] The K-MMSE was developed to maintain the sense of the questions posed in the English MMSE as much as possible and its validity and reliability were verified by Kang et el.[19] K-MMSE scores range from 0 to 30, and lower scores indicate poorer cognition. The K-MMSE awards 5 points for time orientation, 5 points for place orientation, 3 points for registration, 3 points for recall, 5 points for attention and calculation, 8 points for language, and 1 point for visual construction. Cognitive impairment was defined as a K-MMSE score of below 23 points (≤23).[20]

2) The Cardiovascular Health Study Frailty Index

Fried proposed that frailty be defined as a condition meeting at least three of the following five items; weight loss, exhaustion, reduced walking speed, reduced physical activity, and reduced grip strength. Subjects with 1 to 2 positive items are classified as prefrail, and those with no positive item as robust.[4]

(1) Weight loss

Weight loss was defined as unintentional weight loss of >4.5 kg (or 5% of body weight) over the previous year (score = 1).

(2) Exhaustion

Two items from the Center for Epidemiological Studies-Depression scale were used to assess exhaustion: “I feel that everything I do is an effort.” and “I cannot get going.” Subjects answering “yes” at least 3 days per week to either of these two items were assigned one point (score = 1).

(3) Low physical activity

Calories consumed per week were calculated using the International Physical Activity Questionnaire-Short Form, the reliability and validity of which have been demonstrated by domestic and international studies.[21] The cut-off values of physical activity in this study was 462 kcal per week for males and 297 kcal per week for females, which represent the values of the lowest 20% obtained by reanalyzing data collected during the Survey on health and welfare status of the elderly in Korea 2008, which was conducted in 10,715 community-dwelling older Koreans aged ≥ 65 years.[22] Subjects with values lower than the above-mentioned cut-off values were assigned one point (score = 1).

(4) Reduced gait speed

A standard walking speed was set by measuring the time taken to walk 4.5 m. Subjects were asked to walk 6 m at a comfortable walking speed. Times taken to walk 4.5 m, excluding the starting and ending portions of 0.75 m, were measured twice and the shorter time was selected. We adopted cut-off values representing values of the lowest 20% obtained by reanalyzing data collected during the survey on health and welfare status of the elderly in Korea 2008, which was conducted in 10,715 community-dwelling older Koreans aged ≥ 65 years.[22] However, the Survey on health and welfare status of the elderly in Korea 2008 measured times taken to walk 2.5 m. Subjects lower than the cut-off value were assigned one point (score = 1).

(5) Reduced grip strength

Grip strength was measured twice using a dynamometer (JAMAR hydraulic hand dynamometer; Sammons Preston, Bolingbrook, IL, USA). Subjects were asked to grip the dynamometer with lowered straight arms without allowing the dynamometer to touch the body. Hand grip strengths were measured in kg twice and higher values were used in the analysis. We used the cut-off values of the lowest 20% adjusted for sex and body mass index (BMI) obtained by reanalyzing data collected during the survey on health and welfare status of the elderly in Korea 2008, which was conducted in 10,715 community-dwelling older Koreans aged ≥ 65 years using a dynamometer (TANITA Hand Grip Meter Bule 6103; Tanita Co., Tokyo, Japan).[22] Subjects with grip strengths lower than the cut-off value were assigned one point (score = 1).

3) Chronic disease

Chronic diseases were assessed using self reported questionnaires, which including a series of questions about whether they had ever been told by a doctor that they had myocardial infarction (MI), angina, congestive heart failure (CHF), peripheral vascular disease (PVD), arthritis, cancer, diabetes, hypertension, or chronic obstructive pulmonary disease (COPD).

4) Fall

A fall was defined as a state where the body contacted the ground as a result of an unintentional falling. Fall frequency was defined as the number of fall downs experienced over the previous six months.

5) Self-assessed depressive symptoms

The presence of self-assessed depressive symptoms was determined based on responses to the question, "Have you felt depressed or sad during the past month?"

6) Covariates

The covariates included in the analysis were sociodemographic and psychophysical confounders affecting cognitive function,[23-26] that is, gender, age, height, weight, BMI, blood pressure, hospitalization over the previous year, polypharmacy (the use of four or more regular medications), alcohol consumption (history of alcohol drinking in the past one year), smoking (Ever smoker [current or former] / never smoker), cohabiting family members, and years of education.

3. Statistical Analysis

Univariate analysis and multiple linear regression analysis were conducted to examine relations between demographics, CHS Frailty Indices, and K-MMSE scores (dependent variable). The chi-square test, the t-test, and one-way analysis of variance were used for univariate analysis. Correlates were then entered into a multiple regression model. Multiple linear regression analysis included an examination of interaction effects and assessments of possible multicollinearities among independent variables. PASW SPSS ver. 18.0 (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis.

RESULTS

1. General Characteristics

Mean ages were 75.5 ± 5.6 years for males and 74.2 ± 5.8 years for females. Males were taller and heavier than females (164.6

± 5.6 cm and 63.2 ± 8.4 kg for males versus 151.8 ± 5.9 cm and 55.8 ± 8.5 kg for females, P < 0.001), but females had a greater mean BMI (24.2 ± 3.2 kg/m^2 for males versus 23.3 ± 2.9 kg/m^2 for females, P = 0.004). Smoking, drinking, and educational level were higher for males than females, but depression was more frequent in females (15.4% for males and 24.2% for females, P = 0.033). In terms of cohabiting family members, more males lived with a spouse (59.6% for males and 23.7% for females, P < 0.001), whereas more females lived with their offspring or alone. Mean K-MMSE scores were 27.4 ± 2.2 for males and 26.4 ± 3.4

Table 1. General characteristics of the study population

Characteristic	Category	Total (n = 486)	Female (n = 330)	Male (n = 156)	P-value
Age (y)		74.6 ± 5.8	74.2 ± 5.8	75.5 ± 5.6	0.015
Height (cm)		155.9 ± 8.3	151.8 ± 5.9	164.6 ± 5.6	<0.001
Weight (kg)		58.2 ± 9.2	55.8 ± 8.5	63.2 ± 8.4	<0.001
Body mass index		23.9 ± 3.1	24.2 ± 3.2	23.3 ± 2.9	0.004
Blood pressure (mm Hg)	Systolic	134.8 ± 19.8	135.6 ± 19.7	133.0 ± 20.0	0.176
	Diastolic	78.9 ± 11.3	78.4 ± 10.3	80.1 ± 13.2	0.171
No. of chronic disease	None	113 (23.3)	67 (20.3)	46 (29.5)	0.054
	1	194 (39.8)	130 (39.4)	64 (41.0)	
	2	131 (27.0)	99 (30.0)	32 (20.5)	
	≥3	48 (9.9)	34 (10.3)	14 (8.9)	
Recent fall	No	417 (85.8)	278 (84.2)	139 (89.1)	0.166*
	Yes	69 (14.2)	52 (15.8)	17 (10.9)	
Hospital admission	No	400 (82.3)	277 (83.9)	123 (78.8)	0.204
	Yes	86 (17.7)	53 (16.1)	33 (21.2)	
Polypharmacy	≤3	406 (83.5)	272 (82.4)	134 (85.9)	0.362*
	≥4	80 (16.5)	58 (17.6)	22 (14.1)	
Depressive symptom	No	382 (78.6)	250 (75.8)	132 (84.6)	0.033*
	Yes	104 (21.4)	80 (24.2)	24 (15.4)	
Alcohol	No	381 (78.2)	304 (92.1)	77 (49.4)	<0.001
	Yes	105 (21.8)	26 (7.9)	79 (50.6)	
Smoking	No	385 (79.2)	318 (96.4)	67 (42.9)	<0.001
	Yes	101 (20.8)	12 (3.6)	89 (57.1)	
Cohabiting family members	Alone	172 (35.5)	137 (41.6)	35 (22.4)	<0.001
	Spouse	171 (35.3)	78 (23.7)	93 (59.6)	
	Offspring	128 (26.4)	102 (31.0)	26 (16.7)	
	Etc.	14 (2.9)	12 (3.6)	2 (1.3)	
Education (y)	≤6	231 (47.5)	191 (57.9)	40 (25.6)	<0.001
	7–9	93 (19.1)	55 (16.7)	38 (24.4)	
	≥10	162 (33.3)	84 (25.5)	79 (50.0)	
Korean Mini-Mental State Examination		26.7 ± 3.1	26.4 ± 3.4	27.4 ± 2.2	0.001

Values are presented as mean ± SD or numbers (%). P-values were calculated using t-test or chi-square test.
*P-values were calculated using Fisher's exact test.

for females, which was a significant difference (P = 0.001). No significant gender differences were found for blood pressure, number of chronic diseases, fall frequency over the previous six months, hospitalization over the previous year, or polypharmacy (Table 1).

2. The Cardiovascular Health Study Frailty Indices

According to the CHS Frailty Indices, 36 subjects (7.4%) were frail, 244 subjects (50.2%) were prefrail, and 206 subjects (42.4%) were robust. No significant gender-associated differences were found (Table 2).

3. Factors that Affected Cognitive Function

The factors found to affect K-MMSE scores were; gender, age, height, weight, diastolic blood pressure, number of chronic diseases, history of hospital admission, polypharmacy, self-assessed depression, cohabiting family members, education, and CHS Frailty Index. Mean K-MMSE score was higher for males (27.4 ± 2.2 for males and 26.4 ± 3.4 for females, P = 0.001) and scores significantly decreased with age (27.7 ± 1.9 for ≤69 years, 26.9 ± 2.8 for 70 to 79 years, and 25.1 ± 4.2 for ≥80 years; P < 0.001). Furthermore, subjects with a height of <150 cm and subjects with a weight of <51.3 kg had lower mean K-MMSE scores (P < 0.001 and P = 0.001, respectively). Although mean K-MMSE scores were not significantly affected by each chronic disease, such as MI, angina, CHF, PVD, arthritis, cancer, diabetes, hypertension, or COPD, number of chronic disease was related with K-MMSE (P = 0.005). Mean K-MMSE score was higher for subjects with a diastolic blood pressure (BP) of ≥78 mm Hg than for those with a diastolic BP of <71 mm Hg (P = 0.005). Mean K-MMSE score was found to be significantly lower for study subjects with a medical history of hospitalization within the previous six months (P = 0.004) and for those taking at least four medications (P = 0.001). Mean K-MMSE score was significantly lower in study subjects with self-assessed depression (P < 0.001), and in those living alone than in those living with a spouse (P = 0.001). Furthermore, mean K-MMSE score was found to be significantly lower for those that spent less than six years in full-time education (P < 0.001). In addition, difference was shown depend on the groups according to CHS frailty score. Mean K-MMSE score was 27.5 ± 2.2 in the robust group, 26.5 ± 3.1 in the pre-frail, and 23.7 ± 5.3 in the frail group (P < 0.001) (Table 3). Furthermore, when cognitive impairment was defined as a K-MMSE score of below 23 (≤23) points, 6.3% of robust subjects (13 of 206), 16.8% of prefrail subjects (41 of 244), and 30.6% of

Table 2. Distributions of CHS Frailty Indices

Domain	Total (n = 486)	Female (n = 330)	Male (n = 156)	P-value
Weight loss*	62 (12.8)	48 (14.5)	14 (9.0)	0.109†
Exhaustion‡	112 (23.0)	87 (26.4)	25 (16.0)	0.011†
Lowest 20% of physical activity (IPAQ)§,‖	75 (15.4)	57 (17.3)	18 (11.5)	0.108†
Lowest 20% in walking speed§,¶	14 (2.9)	9 (2.7)	5 (3.2)	0.776†
Lowest 20% in grip strength§,**	167 (34.4)	115 (34.8)	52 (33.3)	0.760
CHS frailty criteria				
Robust	206 (42.4)	131 (39.7)	75 (48.1)	0.093
Prefrail	244 (50.2)	170 (51.5)	74 (47.4)	
Frail	36 (7.4)	29 (8.8)	7 (4.5)	

Values are presented as numbers (%). P-values were calculated using t-test or chi-square test.
CHS: Cardiovascular Health Study, BMI: body mass index, IPAQ: International Physical Activity Questionnaire.
*>4.5 kg or 5% weight loss during the last year. †Calculated using Fisher's exact test. ‡A score of 2 or 3 on either question on the Center for Epidemiological Studies-Depression scale. §Cutoff values of the lowest 20% were obtained by reanalyzing data collected during the survey on health and welfare status of the elderly in Korea 2008, which was conducted in 10,715 community-dwelling older Koreans aged ≥ 65 years.[22] ‖Female ≤ 297 kcal/wk; male ≤ 462 kcal/wk. ¶Female: <0.4321 m/s for height < 153 cm; <0.4545 m/s for height ≥153 cm. Male: <0.5000 m/s for height < 165 cm; <0.5495 m/s for height ≥165 cm. **Female: ≤13.5 kg for BMI ≤ 21.82; ≤15 kg for BMI 21.83–23.98; ≤15.5 kg for BMI 23.99–26.16; ≤15.5 kg for BMI ≥ 26.17. Male: ≤22.5 kg for BMI ≤ 21.25; ≤25.0 kg for BMI 21.26–23.20; ≤25.5 kg for BMI 23.21–25.09; ≤26.0 kg for BMI ≥25.10.

Table 3. Distribution of Korean Mini-Mental Status Examination scores

Variable	Category	Mean ± SD	P-value	Post-hoc
Gender	Female	26.4 ± 3.4	0.001*	
	Male	27.4 ± 2.2		
Age (y)	≤69	27.7 ± 1.9	<0.001**	a[†]
	70–79	26.9 ± 2.8		b
	≥80	25.1 ± 4.2		c
Height (cm)	≤149.9	25.2 ± 4.2	<0.001**	a[†]
	150–155.9	26.8 ± 2.8		b
	156–161.9	27.3 ± 2.5		b
	≥162	27.4 ± 2.2		b
Weight (kg)	≤51.2	25.7 ± 3.9	<0.001**	a[†]
	51.3–57.9	26.8 ± 3.1		a, b
	58.0–63.9	27.0 ± 2.4		b
	≥64.0	27.2 ± 2.7		b
Diastolic blood pressure (mm Hg)	≤70	26.1 ± 3.6	0.005**	a[†]
	71–77	26.3 ± 3.5		a, b
	78–84	27.2 ± 2.4		b
	≥85	27.2 ± 2.8		a, b
No. of chronic disease	None	26.8 ± 2.7	<0.005**	a[†]
	1	27.2 ± 2.7		a
	2	26.3 ± 3.3		a
	≥3	25.5 ± 4.5		a
Hospital admission	No	26.9 ± 2.9	0.004*	
	Yes	25.7 ± 3.8		
Polypharmacy	≤3	26.9 ± 2.9	<0.001*	
	≥4	25.8 ± 4.1		
Depressive symptom	No	27.0 ± 2.8	<0.001*	
	Yes	25.6 ± 3.9		
Cohabiting family members	Alone	25.8 ± 3.7	<0.001**	a[†]
	Spouse	27.4 ± 2.3		b
	Offspring	26.8 ± 3.1		a, b
	Etc.	26.7 ± 3.8		a, b
Education (y)	≤6	25.9 ± 3.1	<0.001**	a[†]
	7–9	27.8 ± 1.9		b
	≥10	27.2 ± 3.4		b
Cardiovascular Health Study frailty criteria	Robust	27.5 ± 2.2	<0.001**	a[†]
	Prefrail	26.5 ± 3.1		b
	Frail	23.7 ± 5.3		c

*Calculated using the t-test. **Calculated using one way analysis of variance. [†]Same letters indicate non-significant differences between groups by Tamhane's T2 multiple comparison test.

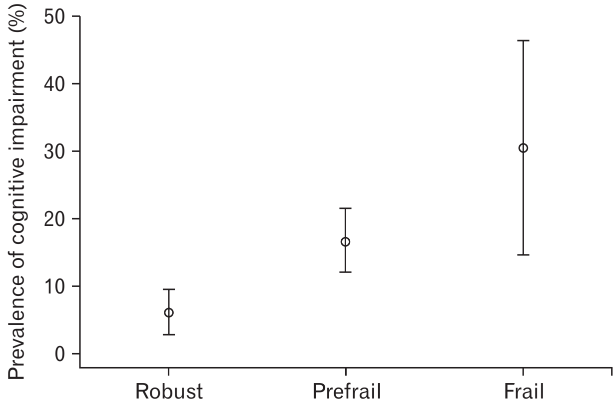

Figure 2. Prevalence of cognitive impairment according to the level of frailty.

Table 4. Relations between variables and K-MMSE scores by multiple linear regression

Variable	K-MMSE score (R^2 = 0.353)		
	B	Standard error	P-value
Male	−0.79	0.38	0.039
Age (y)	−0.08	0.02	<0.001
Education (y)	0.49	0.05	<0.001
Height (cm)	0.06	0.02	0.018
CHS frailty criteria			
Robust	–	–	Reference
Prefrail	−0.41	0.26	0.118
Frail	−1.92	0.52	<0.001
Total CHS frailty score*	−0.69	0.22	0.002

Other covariates (cohabiting family members, number of chronic disease, diastolic blood pressure, weight, hospital admission, polypharmacy, and depressive symptom) were not statistically significant.
K-MMSE: Korean Mini-Mental Status Examination, CHS: Cardiovascular Health Study.
*Multiple regression analysis was also performed using total CHS frailty scores as a continuous independent variable instead CHS frailty criteria.

frail subjects (11 of 36) were found to be cognitive impaired ($P < 0.001$) (Figure 2).

4. Relationship between Cardiovascular Health Study Frailty Indices and Korean Mini-Mental State Examination Scores

Multiple regression analysis was conducted using factors found to be significantly related to cognitive function by univariate analysis to prevent confounding effects. K-MMSE score was defined as the dependent variable, and gender, age, height, weight, diastolic blood pressure, number of chronic diseases, history of hospital admission, polypharmacy, self-assessed depression, family member, education, and CHS frailty criteria were analyzed as independent variables. Frailty was found to be negatively correlated with K-MMSE scores after adjustment for possible confounders (B = -1.92, SE 0.52; $P < 0.001$). However, no association was found between prefrailty and K-MMSE scores. When we also performed multiple regression analysis using total CHS frailty scores as a continuous independent variable instead of CHS frailty criteria, total CHS frailty scores were negatively correlated with K-MMSE scores (B = -0.69, SE 0.22; $P = 0.002$) (Table 4).

DISCUSSION

In this study, physical frailty and cognitive function were found to be negatively correlated in older Koreans (>65 years old) by multiple linear regression analysis after adjusting for other factors, which is in accord with the findings of previous studies.[7,27] However, prefrailty was not found to be associated with lower K-MMSE scores (Table 4). Nevertheless, the prevalence of cognitive impairment (K-MMSE ≤ 23) among prefrail older adults (16.8%) was higher in comparison to robust older adults (6.3%) and substantially lower in comparison to frail older adults (30.6%) (Figure 2). Furthermore, when we performed multiple linear regression analysis to examine association total CHS frailty scores (as a continuous independent variable) with K-MMSE scores, they were also found to be negatively correlated (B = -0.69, SE 0.22; $P = 0.002$) (Table 4). The above mentioned results implicate that the prevention of transition to poorer frail status is important. Espinoza et al. emphasized the significance of prefrailty as a separate risk state because in their longitudinal study, substantially lower mortality was observed in prefrail than in frail individuals.[28] The prefrail individuals are more likely to improve over time than frail individuals, and thus, may be responsive to clinical interventions to slow or reverse worsening of frailty.[28] A recent study conducted in Hong Kong on transition between frailty states among Asians demonstrated that among prefrail older adults at baseline (850 males and 884 females), 23.4% of males and 26.6% of females improved after 2 years, and 11.1% of males and 6.6% of females worsened.[29] In the study, a higher MMSE score was found to be protective among prefrail men, which means cognitive impairment indicates future frailty.[29] This result supports the 'cycle of frailty' hypothesis, which states that frailty may occur as a result of chronic disease, immobility, malnutrition, depression, or dementia, and that frailty may in turn aggravate causal diseases.[4,30-32] However, further longitudinal studies are required to identify the cause-effect relationships between frailty and cognitive function.

Although evidence regarding the effects of interventions targeting frailty coupled with cognitive decline is limited, a small number of studies have shown physical activity confers cognitive benefits.[3] Landi et al.[33] found that physical activity protected against both sarcopenia and cognitive decline in experimental training trials and in observational studies. Furthermore, a recent study demonstrated that a 12-week aerobic exercise and strength training program for frail and non-frail older adults improved functional capacity, physical endurance, cognition, and quality of life.[34] In addition, balance exercises like Tai Chi have been reported to prevent frailty and inhibit its progression in older patients that found muscular strength exercises difficult.[35] Further studies of interventions are needed to confirm that physical activity is beneficial to older people with frailty and cognitive impairment.

The prevalence of frailty in the present study (7.4%) was similar to that reported in previous studies.[4,10,27] Some studies have reported that there were different prevalence of frailty among different ethnicities.[10] However, in one study, when the cut-off values of the domains of the CHS Frailty Indices were modified for ethnic groups, prevalence of frailty were similar.[36] Nevertheless, it should be noted that studies differ with respect to the prevalence of frailty in each domain of the CHS Frailty Indices.[4,10,27] In the present study, a much lower prevalence of frailty was observed in 'reduced gait speed' domain (2.9%) than in other studies (19.9% in Mexican Americans[10] and 20.0% in European Americans[4]). On the other hand, the 34.4% prevalence of reduced grip strength was higher than in other studies (15.4% in Mexican Americans[10] and 20.0 % in European Americans[4]). These differences might have been caused because our study population (n = 486) did not represent the normal older population. For this reason, we adopted cutoff values of the lowest 20% as determined by a large sized study (survey on health and welfare status of the elderly in Korea 2008).[22] On the other hand, in previous studies cutoff values of the lowest 20% in their study populations were used (n = 5,317 in Fried et al.'s study[4] and n = 1,370 in Samper-Ternent et al.'s study[10]), which could represent their normal older populations. Hence, a small number of subjects exhibited reduced gait speed. In addition, we did not consider measurement bias coming from different walk distance to calculate gait speed between our study (4.5 m) and the reference study (2.5 m).[22]

On the other hand, the prevalence of reduced grip strength (34.3%) was higher in the present study than in other studies (15.4% in Mexican Americans[10] and 20.0% in European Americans[4]). It means that grip strength was lower in our study population than in the normal older population. Because grip strength declines with age,[30] this phenomenon could be explained by age distribution. In our study population, there was a lower proportion of subjects aged ≤ 70 years (27.7% vs. 38.0%) and a higher proportion of aged ≥ 80 years old (25.1% vs. 16.0%) than in the normal older population.[22] Furthermore, there is a possibility for bias from different tools used to measure grip strength. The JAMAR hydraulic hand dynamometer (Sammons Preston) was used in our study, but the TANITA Hand Grip Meter Bule 6103 (Tanita Co.) was used in the reference study (Survey on health and welfare status of the elderly in Korea 2008).[22]

The prevalence of frailty depends on the domain cutoff values used for physical activity, gait speed, grip strength, and others. The most appropriate cutoff values for reduced gait speed and reduced grip strength are important issues that remain to be resolved in the sarcopenia field. The guidelines issued by the European Working Group on Sarcopenia in Older People in 2010 suggest a cutoff value of <0.8 m/s be used for low gait speed, and that cutoff values of <30 kg for males and <20 kg for females be used to determine reduced grip strength.[37] A large scale of study on sarcopenia in the US, Foundation for the National Institutes of Health (FNIH) Sarcopenia Project conducted in 2014 recommended cutoff values for grip strength < 26 kg for male and <16 kg for female.[38] However, the study population of the FNIH Sarcopenia Project was predominantly Caucasian (90%), and thus, it is questionable whether it can be applied to other different ethnicities. Further studies are required to determine cutoff values with high sensitivity and specificity to screen for frailty and sarcopenia.

Limitations of this study required consideration. First, the representativeness of study populations recruited from community senior welfare centers is questionable. However, we used representative cutoff values obtained by reanalyzing data of a large number study (survey on health and welfare status of the elderly in Korea 2008).[22] Second, we were not able to investigate cause-effect relationships between frailty and cognitive function due to the cross-sectional nature of the study. Third, self-assessed depression might be inaccurate as no physician assessments were performed, and depression is an important consideration because it can mimic cognitive impairment. Fourth, we analyzed only total K-MMSE scores, but some study assessed that association frailty with the each domain of MMSE and reported that being frail was related with worse performance in domains of MMSE such as time orientation, immediate memory, and the ability to follow commands.[27] Nevertheless, the present study is the first study to describe the association between frailty and cognitive function in older Koreans.

In conclusion, this study shows that frailty is associated with cognition impairment in older Koreans. However, prospective cohort studies are required to provide higher levels of evidence.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

ACKNOWLEDGEMENTS

We would like to thank The Senior Functional Assessment Research Group of The Korean Geriatrics Society for collecting the data.

REFERENCES

1. Korea Institute for Health and Social Affairs. A base study for 2008 living profiles and welfare service needs of older persons in Korea's survey. Seoul: Korea Institute for Health and Social Affairs; 2008.
2. Statistics Korea. Population projections for Korea. Daejeon: Statistics Korea; 2006.
3. Robertson DA, Savva GM, Kenny RA. Frailty and cognitive impairment: a review of the evidence and causal mechanisms. Ageing Res Rev 2013;12:840-51.
4. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56:M146-56.
5. Rockwood K, Fox RA, Stolee P, Robertson D, Beattie BL. Frailty in elderly people: an evolving concept. CMAJ 1994;150:489-95.
6. Allegri RF, Glaser FB, Taragano FE, Buschke H. Mild cognitive impairment: believe it or not? Int Rev Psychiatry 2008;20:357-63.
7. Avila-Funes JA, Amieva H, Barberger-Gateau P, Le Goff M, Raoux N, Ritchie K, et al. Cognitive impairment improves the predictive validity of the phenotype of frailty for adverse health outcomes: the three-city study. J Am Geriatr Soc 2009;57:453-61.
8. Auyeung TW, Lee JS, Kwok T, Woo J. Physical frailty predicts future cognitive decline: a four-year prospective study in 2737 cognitively normal older adults. J Nutr Health Aging 2011;15:690-4.
9. Mitnitski A, Fallah N, Rockwood MR, Rockwood K. Transitions in cognitive status in relation to frailty in older adults: a comparison of three frailty measures. J Nutr Health Aging 2011;15:863-7.
10. Samper-Ternent R, Al Snih S, Raji MA, Markides KS, Ottenbacher KJ. Relationship between frailty and cognitive decline in older Mexican Americans. J Am Geriatr Soc 2008;56:1845-52.
11. Buchman AS, Boyle PA, Wilson RS, Tang Y, Bennett DA. Frailty is associated with incident Alzheimer's disease and cognitive decline in the elderly. Psychosom Med 2007;69:483-9.
12. Solfrizzi V, Scafato E, Frisardi V, Seripa D, Logroscino G, Maggi S, et al. Frailty syndrome and the risk of vascular dementia: the Italian Longitudinal Study on Aging. Alzheimers Dement 2013;9:113-22.
13. Sourial N, Bergman H, Karunananthan S, Wolfson C,

Guralnik J, Payette H, et al. Contribution of frailty markers in explaining differences among individuals in five samples of older persons. J Gerontol A Biol Sci Med Sci 2012;67:1197-204.
14. Sourial N, Wolfson C, Bergman H, Zhu B, Karunananthan S, Quail J, et al. A correspondence analysis revealed frailty deficits aggregate and are multidimensional. J Clin Epidemiol 2010;63:647-54.
15. Hwang HS, Kwon IS, Park BJ, Cho B, Yoon JL, Won CW. The validity and reliability of Korean Frailty Index. J Korean Geriatr Soc 2010;14:191-202.
16. Hwang HS, Yoon JL, Park BJ, Choi HR, Kwon IS, Shinkai S, et al. The validity and reliability of the Kaigo-Yobo checklist in Korean elderly. J Korean Geriatr Soc 2012;16:121-32.
17. Ferrucci L, Guralnik JM, Studenski S, Fried LP, Cutler GB Jr, Walston JD, et al. Designing randomized, controlled trials aimed at preventing or delaying functional decline and disability in frail, older persons: a consensus report. J Am Geriatr Soc 2004;52:625-34.
18. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-98.
19. Kang Y, Na DL, Hahn S. A validity study on the Korean Mini-Mental State Examination (K-MMSE) in dementia patients. J Korean Neurol Assoc 1997;15:300-8.
20. Kang MA, Baek YM. The neurocognitive function between the patients who had subjective memory impairment and mild cognitive impairment. J Korean Geriatr Soc 2014;18:7-15.
21. Oh JY, Yang YJ, Kim BS, Kang JH. Validity and reliability of Korean version of International Physical Activity Questionnaire (IPAQ) short form. J Korean Acad Fam Med 2007;28:532-41.
22. Ministry of Health and Welfare. Survey on health and welfare status of the elderly in Korea 2008 [Internet]. Seoul: Ministry of Health and Welfare; c2012 [cited 2009 Jul 13]. Available from: http://www.mw.go.kr/.
23. Bird HR, Canino G, Stipec MR, Shrout P. Use of the Mini-mental State Examination in a probability sample of a Hispanic population. J Nerv Ment Dis 1987;175:731-7.
24. Escobar JI, Burnam A, Karno M, Forsythe A, Landsverk J, Golding JM. Use of the Mini-Mental State Examination (MMSE) in a community population of mixed ethnicity: cultural and linguistic artifacts. J Nerv Ment Dis 1986;174:607-14.
25. Magaziner J, Bassett SS, Hebel JR. Predicting performance on the Mini-Mental State Examination: use of age- and education-specific equations. J Am Geriatr Soc 1987;35:996-1000.
26. O'Connor DW, Pollitt PA, Treasure FP, Brook CP, Reiss BB. The influence of education, social class and sex on Mini-Mental State scores. Psychol Med 1989;19:771-6.
27. Macuco CR, Batistoni SS, Lopes A, Cachioni M, da Silva Falcao DV, Neri AL, et al. Mini-Mental State Examination performance in frail, pre-frail, and non-frail community dwelling older adults in Ermelino Matarazzo, Sao Paulo, Brazil. Int Psychogeriatr 2012;24:1725-31.
28. Espinoza SE, Jung I, Hazuda H. Frailty transitions in the San Antonio Longitudinal Study of Aging. J Am Geriatr Soc 2012;60:652-60.
29. Lee JS, Auyeung TW, Leung J, Kwok T, Woo J. Transitions in frailty states among community-living older adults and their associated factors. J Am Med Dir Assoc 2014;15:281-6.
30. Gill TM, Williams CS, Tinetti ME. The combined effects of baseline vulnerability and acute hospital events on the development of functional dependence among community-living older persons. J Gerontol A Biol Sci Med Sci 1999;54:M377-83.
31. Sager MA, Franke T, Inouye SK, Landefeld CS, Morgan TM, Rudberg MA, et al. Functional outcomes of acute medical illness and hospitalization in older persons. Arch Intern Med 1996;156:645-52.
32. Wu AW, Yasui Y, Alzola C, Galanos AN, Tsevat J, Phillips RS, et al. Predicting functional status outcomes in hospitalized patients aged 80 years and older. J Am Geriatr Soc 2000;48(5 Suppl):S6-15.
33. Landi F, Abbatecola AM, Provinciali M, Corsonello A, Bustacchini S, Manigrasso L, et al. Moving against frailty: does physical activity matter? Biogerontology 2010;11:537-45.
34. Langlois F, Vu TT, Chasse K, Dupuis G, Kergoat MJ, Bherer L. Benefits of physical exercise training on cognition and quality of life in frail older adults. J Gerontol B Psychol Sci Soc Sci 2013;68:400-4.

35. Wolf SL, Barnhart HX, Kutner NG, McNeely E, Coogler C, Xu T. Reducing frailty and falls in older persons: an investigation of Tai Chi and computerized balance training. Atlanta FICSIT Group. Frailty and Injuries: Cooperative Studies of Intervention Techniques. J Am Geriatr Soc 1996;44:489-97.
36. Espinoza SE, Hazuda HP. Frailty in older Mexican-American and European-American adults: is there an ethnic disparity? J Am Geriatr Soc 2008;56:1744-9.
37. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: report of the European Working Group on Sarcopenia in Older People. Age Ageing 2010;39:412-23.
38. Studenski SA, Peters KW, Alley DE, Cawthon PM, McLean RR, Harris TB, et al. The FNIH sarcopenia project: rationale, study description, conference recommendations, and final estimates. J Gerontol A Biol Sci Med Sci 2014;69:547-58.